What is claimed is:

1. A method for drug discovery, said method comprising: (A) constructing one or more protein-fragment complementation assays (PCAs'); (B) testing the effects of chemical compounds on the activity of said assay(s); (C) using the results of said assay(s) to identify chemical compounds with desired activities.

2. A method of screening chemical compounds, said method comprising: (A) constructing protein-fragment complementation assays for one or more steps in a cellular pathway; (B) testing the effects of said compounds on the activity of said assay(s); (C) using the results of said screen to identify compounds that activate or inhibit the cellular pathway(s) of interest.

3. A method of screening chemical compounds, said method comprising: (A) selecting a chemical library; (B) constructing one or more protein-fragment complementation assay(s); (C) testing the effects of chemical compounds from said library on said assay(s); (C) using the results of said screen to identify specific compounds that increase or decrease the signal generated in said assay(s).

4. A method of screening chemical compounds, said method comprising: (A) selecting a chemical library; (B) constructing one or more protein-fragment complementation assay(s); (C) testing the effects of chemical compounds from said library on said assay(s); (C) using the results of said screen to identify specific compounds which alter the subcellular location of the signal generated in said assay(s).

5. A method for constructing an assay, said method comprising:

(a) selecting genes encoding proteins that interact ;

(b) selecting an appropriate reporter molecule;

(c) effecting fragmentation of said reporter molecule such that said fragmentation results in reversible loss of reporter function;

(d) fusing or attaching fragments of said reporter molecule separately to other molecules;

(e) reassociating said reporter fragments through interactions of the molecules that are fused or attached to said fragments; and

(f) measuring the activity of said reporter molecule with automated instrumentation.

6. A method according to Claim 5 whereby the reporter molecule is selected from the group consisting of an enzyme, a fluorescent protein, a luminescent protein, a phosphorescent protein, a monomeric protein, an antigen, or an antibody.

7. A method according to Claims 1, 2, 3, 4, 5 or 6 whereby the reporter fragments are created by oligonucleotide synthesis, by fragmenting an intact reporter molecule, or by DNA amplification of a template.

8. A method according to claim 1 wherein an optically detectable signal is generated in the assay.

9. A method according to claim 1 wherein the signal generated in the assay is fluorescence, bioluminescence, chemiluminescence, or phosphorescence.

10. A method according to claim 1 whereby the assay is performed in multiwell formats, in microtiter plates, in multispot formats, or in arrays.

11. A method according to claim 1, 2, 3, 4, 5 or 6 whereby the assay is performed by fluorescence spectrometry, luminescence spectrometry, fluorescence activated cell analysis, fluorescence activated cell sorting, automated microscopy or automated imaging.

12. A method according to claim 1 whereby the assay is performed in live cells, in fixed cells, or in cell lysates.

13. A method according to claim 1 whereby the molecules fused to the reporter fragments of the PCA are identified by a method chosen from the group consisting of: (a) cDNA

library screening; (b) interaction mapping; and (c) prior knowledge of the existence of an interaction between a pair of proteins.

14. A method according to Claim 1 wherein the subcellular distribution of the assay signal and/or the intensity of the assay signal is determined.

15. A method according to Claim 5 wherein the reporter is a dihydrofolate reductase, a beta-lactamase, a luciferase, a green fluorescent protein, or a yellow fluorescent protein.

16. A method according to Claims 1 wherein said chemical compounds are selected from the group consisting of synthetic molecules, known drugs, natural products, peptides, nucleic acids, antibodies, and small interfering RNAs.

17. Protein fragment complementation assays for drug discovery comprising a reassembly of separate fragments of a reporter molecule wherein reassembly of the reporter fragments generates an optically detectable signal.

18. Protein fragment complementation assays for drug discovery wherein the assay signal is detected with automated instrumentation.

19. Assays according to Claim 17 wherein the reporter molecule is selected from the group consisting of an enzyme, a fluorescent protein, a luminescent protein, a phosphorescent protein, a monomeric protein, an antigen, or an antibody.

20. Assays according to Claim 17 or Claim 18 wherein the assay signal is fluorescence, bioluminescence, chemiluminescence, or phosphorescence.

21. Assays according to Claim 17 wherein said assays are performed in multiwell formats, in microtiter plates, in multispot formats, or in arrays.

22. Assays according to Claim 17 whereby said assays are performed by fluorescence spectrometry, luminescence spectrometry, fluorescence activated cell analysis, fluorescence activated cell sorting, automated microscopy or automated imaging.

23. Assays according to Claim 17 whereby said assays are performed in live cells, in fixed cells, or in cell lysates.

24. Assays according to Claim 17 wherein the subcellular distribution of the assay signal and/or the intensity of the assay signal is determined.

25. Assays according to Claim 17 wherein the reporter is a dihydrofolate reductase, a lactamase, a luciferase, a green fluorescent protein, or a yellow fluorescent protein.

26. An assay composition for drug discovery comprising complementary fragments of a first reporter molecule, said complementary fragments exhibiting a detectable activity when associated, wherein each fragment is fused to a separate molecule.

27. An assay composition for drug discovery comprising a product selected from the group consisting of:

(a) a first fusion product comprising:

1) a first fragment of a first reporter molecule whose fragments exhibit a detectable activity when associated and

2) a second molecule that is fused to said first fragment;

(b) a second fusion product comprising

1) a second fragment of said first reporter molecule and

2) a third molecule that is fused to said second fragment; and

c) both (a) and (b).

28. An assay composition for drug discovery comprising a product selected from the group consisting of:

(a) a first fusion product comprising:

1) a first fragment of a first reporter molecule whose fragments exhibit a detectable activity when associated and

2) a second molecule that is fused to said first fragment;

(b) a second fusion product comprising

1) a second fragment of said first reporter molecule and

2) a third molecule that is fused to said second fragment; and

c) both (a) and (b).

29. An assay composition for drug discovery comprising a nucleic acid molecule coding for a reporter fragment fusion product, which molecule comprises sequences coding for a product selected from the group consisting of:

(a) a first reporter fusion product comprising:

1) fragments of a first reporter molecule whose fragments can exhibit a detectable activity when associated and

2) a second molecule fused to the fragment of the first molecule;

(b) a second fusion product comprising

1) a second fragment of said first reporter molecule and

2) a second or third molecule; and

(c) both (a) and (b).

30. An assay composition for drug discovery comprising a product selected from the group consisting of:

(a) a first fusion product comprising:

1) a first fragment of a first reporter molecule whose fragments exhibit a detectable activity when associated and

2) a second molecule that is fused to said first fragment;

(b) a second fusion product comprising

1) a second fragment of said first reporter molecule and

2) a third molecule that is fused to said second fragment; and

(c) a third fusion product comprising:

1) a first fragment of a second reporter molecule whose fragments exhibit a detectable activity when associated and

2) a fourth molecule that is fused to said first fragment;

(d) a fourth fusion product comprising

1) a second fragment of said second reporter molecule and

2) a fifth molecule that is fused to said second fragment; and

e) a combination of (a) , (b), (c) and (d).

31. An assay composition for drug discovery comprising a nucleic acid molecule coding for a reporter fragment fusion product, which molecule comprises sequences coding for a product selected from the group consisting of:

(a) a first reporter fusion product comprising:

1) fragments of a first reporter molecule whose fragments can exhibit a detectable activity when associated and

2) a second molecule fused to the fragment of the first molecule;

(b) a second fusion product comprising

1) fragments of a second reporter molecule whose fragments can exhibit a detectable activity when associated and

2) a third molecule fused to the fragment of the second molecule; and

(c) both (a) and (b).

32. An assay composition for drug discovery comprising an expression vector containing at least one molecule of interest that is operably linked to a reporter fragment.

33. An assay composition for drug discovery comprising an expression vector containing (a) a constitutive or an inducible promoter and (b) a gene of interest operably linked to a reporter fragment.

34. An assay composition for drug discovery comprising at least one expression vector containing (a) a first molecule of interest that is operably linked to a fragment of a first reporter, and (b) a second molecule that is operably linked to a fragment of a second reporter.

35. An assay composition according to any one of claim 26 wherein one or more reporter fragment(s) are derived from the group consisting of a fluorescent protein, a bioluminescent protein, a chemiluminescent protein, a phosphorescent protein, an enzyme, a monomeric protein, an antibody and an antigen.

36. A method, assay or composition according to any one of claims 1, 17, or 26 wherein at least one of the molecules fused to a reporter fragment is selected from the group consisting of a receptor, a tumor suppressor gene, a kinase, a kinase substrate, an oncogene, an adaptor protein, a ubiquitin-like molecule, and a transcription factor.

37. A method, assay or composition according to any one of claims 1, 17 or 26 wherein at least one of the molecules fused to a reporter fragment is selected from the group consisting of p53, Chk1, ATR, ATM, Rad 51, PDK2, STAT1, FKBP, FRAP, p70S6Kinase, S6 protein, 4E-BP1, PPP2A, TNFR, TRADD, FADD, p65 subunit of NFkappaB, p50 subunit of NFkappaB, CBP, TRAF2, Ubiquitin, IKK-beta, IKK-gamma, IkappaBalpha, MEK, ERK, PI-3-Kinase, PKB, Ft1, GCN4, PDK1, GSK3, NF-AT, and Calcineurin; and domains, fragments or homologues thereof.

38. A method according to Claim 2 wherein the pathway is a DNA damage response pathway, a receptor tyrosine kinase pathway, a cytokine-dependent pathway, a nutrient-activated pathway, a proteasome pathway, a growth factor-dependent pathway, a mitogen-activated pathway, a hormone-dependent pathway, a heat shock protein pathway, a ubiquitin pathway, a cell cycle pathway, a T-cell pathway or an apoptotic pathway.

39. A method, assay or composition according to any one of Claims 1, 17, or 26 whereby the assay is used to screen for a receptor agonist, a receptor antagonist, a kinase inhibitor, a phosphatase inhibitor, a cell cycle inhibitor, a heat shock protein inhibitor, an E3 ligase inhibitor, a transcription factor inhibitor, an inhibitor of a protein-protein interaction, or a proteasome inhibitor.